REMARKS

Claims 1, 9, 14 and 15 are amended herein and claim 8 is canceled. Support for the amendment is found, for example, at page 14, lines 11-18; page 15, lines 6-14; and page 17, lines 16-22. No new matter is presented.

I. Information Disclosure Statement (IDS)

Applicants note that copies of the PTO/SB/08 Forms submitted with the IDS filed January 23, 2007, are attached to the Action dated October 3, 2007, which have no information and which have been crossed out by the Examiner. An IDS was submitted on October 22, 2007 citing the references that should have been listed on the PTO/SB/08 Form submitted with the IDS on January 23, 2007. Applicants respectfully request the Examiner to acknowledge and return an initialed copy of the PTO/SB/08 Form submitted with the IDS on October 22, 2007 with the next response.

II. Response to Rejection under 35 U.S.C. § 112, first paragraph

On page 2 of the Action, claims 1-3 and 6-14 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for compounds of claim 1 where Y is alkyl or alklene, R^1 is alkyl or cyclo alkylphenyl and R^2 and R^3 are, e.g. pyran, morpholine, thiomorpholine and pyridine, allegedly does not reasonably provide enablement for the broader scope of all hydrocarbons, heterocyclic groups.

Claim 1 is amended herein to further define the hydrocarbon and heterocyclic groups for the "Y" variable, thereby obviating this ground for rejection.

On page 6 of the Action, claims 8 and 9 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for making salts of the claimed

compounds, allegedly does not reasonably provide enablement for making prodrugs of the claimed compounds.

Claim 8 is canceled and the phrase "prodrug thereof" is deleted from claim 9, thereby obviating this ground for rejection.

On page 9 of the Action, claims 9-15 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for having vanilloid receptor against agonist activity with example 51 and treating overactive bladder with example 51, allegedly it does not reasonably provide enablement for preventing overactive bladder, analgesic or vanilloid receptor agonist activity for all known hydrocarbon and/or all heterocyclic substituted compounds of formula (I).

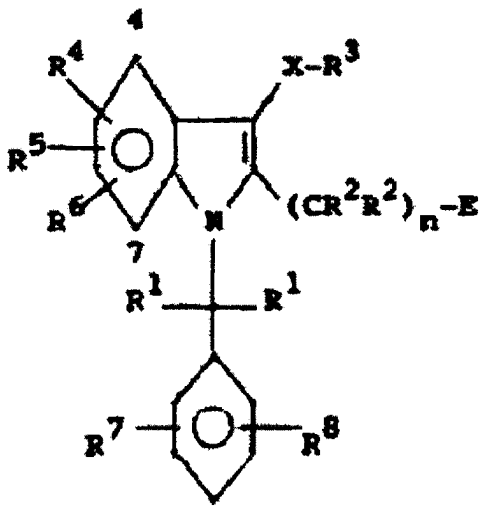
Claims 9-15 depend directly, or indirectly, from claim 1 and claim 1 is amended herein to further define formula (I). Additionally, claim 14 is amended to delete the phrase "preventing and/or". Thus, Applicants submit that the amendments to the claims obviate this ground for rejection.

Accordingly, Applicants respectfully request withdrawal of the §112, first paragraph rejections.

III. Response to Rejection under 35 U.S.C. § 103(a)

On page 12 of the Action, claims 1-13 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Gillard et al (EP 0275667) in view of Arya et al. (US 3954757).

On page 4, Gillard et al (EP-A-0275667) discloses the compound of formula (I) having the following structure:



The structure of this compound is completely different from the present compounds of formula (I) having a condensed ring structure with pyridyl.

Additionally, the compounds disclosed by Gillard et al have a different activity than the compounds of the present invention. At page 3, lines 31-54, Gillard et al. discloses that the above compound has activity as leukotriene biosynthesis inhibitors and has the following effects:

> The present invention relates to compounds having activity as leukotriene biosynthesis inhibitors, to methods for their preparation, and to methods and pharmaceutical formulations for using these compounds in mammals (especially humans).
>
> Because of their activity as leukotriene biosynthesis inhibitors, the compounds of the present invention are useful as anti-asthmatic, anti-allergic, and anti-inflammatory agents and are useful in treating allergic rhinitis and chronic bronchitis and for amelioration of skin diseases like psoriasis and atopic eczema. These compounds are also useful to inhibit the pathologic actions of leukotrienes on the cardiovascular and vascular systems for example, actions such as result in angina or endotoxin shock. The compounds of the present invention are useful in the treatment of inflammatory and allergic diseases of the eye, including allergic

conjunctivitis. The compounds are also useful as cytoprotective agents and for the treatment of migraine headache.

Thus, the compounds of the present invention may also be used to treat or prevent mammalian (especially, human) disease states such as erosive gastritis; erosive esophagitis; inflammatory bowel disease; ethanol-induced hemorrhagic erosions; hepatic ischemic; noxious agent induced damage or necrosis of hepatic, pancreatic, renal, or myocardial tissue; liver parenchymal damage caused by hepatoxic agents such as $CC1_4$ and D-galactosamine; ischemic renal failure; disease-induced hepatic damage; bile salt induced pancreatic or gastric damage; trauma- or stress-induced cell damage; and glycerol-induced renal failure.

The compounds of this invention are inhibitors of the biosynthesis of 5-lipoxygenase metabolites of arachidonic acid, such as 5-HPETE, 5-HETE and the leukotrienes. Leukotrienes B_4, C_4, D_4 and E_4 are known to contribute to various disease conditions such as asthma, psoriasis, pain, ulcers and systemic anaphylaxis. Thus inhibition of the synthesis of such compounds will alleviate these and other leukotriene-related disease states.

At page 7, lines 11-24, Gillard et al further discloses:

The ability of the compounds of Formula I to inhibit biosynthesis of the leukotrienes makes them useful for inhibiting the symptoms induced by the leukotrienes in a human subject. This inhibition of the mammalian biosynthesis of leukotrienes indicates that the compounds and pharmaceutical compositions thereof are useful to treat, prevent, or ameliorate in mammals and especially in humans: 1) pulmonary conditions including diseases such as asthma, 2) allergies and allergic reactions such as allergic rhinitis, contact dermatitis, allergic conjunctivitis, and the like, 3) inflammation such as arthritis or inflammatory bowel disease, 4) pain, 5) skin conditions such as psoriasis and the like, and 6) cardiovascular conditions such as angina, endotoxin shock, and the like, and that the compounds are cytoprotective agents.

The cytoprotective activity of a compound may be observed in both mammals and man by noting the increased resistance of the gastrointestinal mucosa to the noxious effects of strong irritants, for example, the ulcerogenic effects of aspirin or indomethacin. In addition to lessening the effect of non-steroidal anti-inflammatory drugs on the gatrointestinal tract, animal studies show that

> cytoprotective compounds will prevent gastric lesions induced by oral administration of strong acids, strong bases, ethanol, hypertonic saline solutions and the like.

In contrast, the present invention is based on the finding that the specific pyrrolopyridine derivative has vanilloid receptor agonist activity and is useful as a medicine such as an agent for preventing and/or treating overactive bladder or an analgesic (see the Test Examples in the specification as originally filed).

The activity of the compounds of Gillard et al as leukotriene biosynthesis inhibitors is completely different in mechanism from the vanilloid receptor agonist activity of the compounds of the present invention. Though the effect of the compounds of Gillard et al partially overlaps with the effect of the present invention because Gillard et al exemplifies pain as a subject disease for anti-inflammatory activity, the basic technical concepts of the respective inventions are completely different from each other. That is, Gillard et al is based on the inhibitory activity of leukotrienes B_4, C_4, D_4 and E_4, which are substances that cause pain, whereas the present invention is based on vanilloid receptor agonist activity.

Arya et al (US 3,954,757) describes that the disclosed condensed pyrrole mercapto compounds having a specific chemical structure show primarily vasoconstrictor activity in addition to ophthalmological and hypotensive activities, in particular, are useful as a decongestant, e.g., a nasal decongestant (see, column 3, line 63 - column 4, line 4).

Ayra et al seem to disclose compounds wherein Ar has a pyridine ring for example at column 1, lines 25-49, but in Examples, they disclose only indol-related compounds. There is no Example of a compound having pyrrolopyridine structure in this reference.

Furthermore, Ayra et al do not describe the mechanisms of hypotensive and

vasoconstrictor activities, and, there is no Test Example demonstrating the pharmacological effects. Thus, one of ordinary skill in the art would not have had a reasonable expectation of success in achieving the present invention based on the disclosure of Araya et al.

Further, since Ayra et al are different from the present invention in not only chemical structure but also in pharmacological effect and use (subject diseases), it is clear that Ayra et al does not teach or suggest the present invention. Thus, even if Gillard et al and Arya et al are combined, they do not teach or suggest the present invention. Also, since their mechanisms are different from that of the present invention, there is no motivation for combining them to arrive at the present invention. Thus, the present invention is patentable over the cited references, whether taken alone or in combination.

Accordingly, Applicants respectfully request withdrawal of the §103 rejection.

IV. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

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